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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/720,533	03/20/2001	Preeti Lal	PF-0541 USN	2358

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Incyte Genomics Inc
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EXAMINER
LANDSMAN, ROBERT S

ART UNIT	PAPER NUMBER
1647	8

DATE MAILED: 06/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/720,533	LAL ET AL.	
	Examiner	Art Unit	
	Robert Landsman	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-44* is/are pending in the application.

4a) Of the above claim(s) *21-29,31,32 and 36-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-29,31,32 and 36-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Comparisons A-E*

12/16/03

DETAILED ACTION

1. Formal Matters

A. The Information Disclosure Statement, filed 5/27/03, has been entered into the record.

B. Claims 1-20 were pending in this application and were subject to restriction in Paper No.5 dated 4/23/03. In Paper No. 7, Applicants elected Group I with traverse and further elected SEQ ID NO:120 and 254. Applicants cancelled claims 1-20 and added new claims 21-44. Group I corresponds to new claims 21-29, 31, 32 and 36-38. Applicants argue that the antibody of claim 30 should be rejoined. However, a search of the protein of the invention would not overlap a search of the antibody to the protein as different databases are searched for each of these distinct molecules. Furthermore, Applicants have already received method claims drawn toward a method of treating a disease. However, if the present invention is found to be allowable, then method claims which are commensurate in scope with the elected invention and do not raise any issues under 35 USC 112 will be rejoined. This restriction is deemed proper and is, therefore, made FINAL.

2. Information Disclosure Statement

A. All References (1-5) on the Form PTO-1449 have been lined through since none provide a submission date of the Deposit. It is suggested that a new 1449 be submitted which recites the deposit dates for each of these clones. The Examiner did not wish to complete this citation in fear of citing an incorrect deposit date.

3. Priority Data

A. The specification is objected to since there is no claim to priority to PCT/US99/14484 in the first line of the specification. In addition, it is brought to Applicants' attention that the Bibliographic Data Sheet does not recite a claim to priority of the provisional applications as recited in the first line of the specification. Applicant can either request a new Filing Receipt, or this can be dealt with if the claims are found allowable.

4. Claim Objections

A. Claims 22-29, 32, 36 and 37 are objected to since they should recite "the" instead of "a." For example, claims 22 and 25 should recite "The isolated polypeptide..." Claims 23 and 24 should recite "encoding the polypeptide..."

5. Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

A. Claims 21-29, 31, 32 and 36-38 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by a specific, substantial and credible asserted utility or a well established utility. These claims are directed to a polypeptide of SEQ ID NO:120, or a fragment thereof, or encoded by SEQ ID NO:254, or a fragment thereof as well as host cells, methods of making the polypeptide, compositions and methods of using these compounds. However, the invention encompassed by these claims has no apparent or disclosed patentable utility. This rejection is consistent with the current utility guidelines, published 1/5/01, 66 FR 1092. The instant application has provided a description of an isolated protein. However, the instant application does not disclose a specific and substantial biological role of this protein or its significance.

However, it is clear from the instant specification that the claimed receptor is what is termed an "orphan receptor" in the art. The instant application does not disclose the biological role of the claimed protein or its significance. Applicants disclose in the specification that the claimed receptor is believed to be a human signal peptide-containing protein. However, the basis that the receptor of the present invention is a signal peptide-containing protein is not predictive of a use. There is little doubt that, after complete characterization, this protein will probably be found to have a patentable utility. This further characterization, however, is part of the act of invention and, until it has been undertaken, Applicants' claimed invention is incomplete.

The instant claims are drawn to a polynucleotide encoding a protein which has a yet undetermined function or biological significance. There is no actual and specific significance which can be attributed to said protein identified in the specification. For this reason, the instant invention is incomplete. In the absence of a knowledge of the natural ligands or biological significance of this protein, there is no immediately obvious patentable use for it. To employ a protein of the instant invention in the identification of substances which bind to and/or mediate activity of the said receptor is clearly to use it as the object of further research which has been determined by the courts to be a non-patentable utility. Since the instant specification does not disclose a "real-world" use for said protein then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. 101 as being useful.

Furthermore, since the polypeptide of the invention is not supported by a specific and substantial asserted utility or a well established utility, the polynucleotide, host cells, methods of making the polypeptide, compositions and methods of using these compounds also lack utility.

6. Claim Rejections - 35 USC § 112, first paragraph - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. Claims 21-29, 31, 32 and 36-38 are rejected under 35 U.S.C. 112, first paragraph, as failing to adequately teach how to use the instant invention. Specifically, since the claimed invention is not supported by a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

B. Furthermore, if the present invention was found to have utility, claims 21-29, 31, 32 and 36-38 would still be rejected under 35 U.S.C. 112, first paragraph, because the specification, while then being enabling for SEQ ID NO:120 and 254, does not reasonably provide enablement for polynucleotides encoding "**biologically active**" or "**immunogenic**" fragments of SEQ ID NO:120, those which are "**at least 90% identical**" to SEQ ID NO:120 or 254, or for those comprising "**at least 60 contiguous nucleotides**" of SEQ ID NO:254. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

First, the breadth of the claims is excessive with regard to claiming all polypeptides or polynucleotides which are "at least 90%" identical to SEQ ID NO:120 or 254, or for "biologically active" or "immunogenic" fragments of SEQ ID NO:120. Polynucleotides which are 90% identical to, or comprise at least 60 contiguous bases SEQ ID NO:254 would have one or more nucleic acid substitutions,

deletions, insertions and/or additions to said polynucleotide. Similarly, polypeptides which are at least 90% identical to, or are fragments of, SEQ ID NO:120 would encode for a protein with one or more amino acid substitutions, deletions, insertions and/or additions to the protein encoded for by SEQ ID NO:120.

Applicants provide no guidance or working examples of polypeptides or polynucleotides which are of any length other than that of the full-length of SEQ ID NO:120 or 254, including molecules which are at least 90% identical to SEQ ID NO:120 or 254, or fragments thereof, nor do they provide a *function* of these nucleic acid molecules, or of the proteins and fragments which they encode. Furthermore, it is not predictable to one of ordinary skill in the art what the functions of these polynucleotides, or polypeptides are. Applicants have not taught which amino acids or nucleic acids are critical for function of the molecule. For example, there is no teachings of what amino acids are required to maintain the "biological activity" of any protein other than the full-length protein of SEQ ID NO:120. Finally, it is not predictable to the artisan how to make a functional polypeptide or polynucleotide which is less than the full-length of SEQ ID NO:120 or 254 since it is not predictable which residues or nucleic acids are critical for function of the molecule.

In summary, the breadth of the claims is excessive with regard to Applicants claiming all polypeptide and polynucleotides which are less than the full-length of SEQ ID NO:120 or 254, including those which are at elast 90% identical to these molecules as well as biologically active or immunogenic fragments thereof. There is also a lack of guidance and working examples of these polypeptides and polynucleotides. Applicants do not provide a function of these polypeptides or polynucleotides which are other than the full-length molecules, nor do they provide any guidance as to which residues or nucleic acids are required to maintain function of these molecules. These factors, along with the lack of predictability to one of ordinary skill in the art as to how to make and use a functional polypeptide or polynucleotide other than the full-length molecules, leads the Examiner to hold that undue experimentation is necessary to practice the invention as claimed.

C. Similarly, claims 36-38 would not be enabled insofar as they read on compositions in a "**pharmaceutically acceptable carrier**", or a method of "**treating a disease or condition**" associated with all "**HSPP**s." First, the breadth of the claims is excessive since the claims read on all pharmaceutical compositions to treat all diseases associated with the decrease in any and all HSPP expression. First, Applicants have not provided any guidance and working examples of any HSPP proteins other than that of SEQ ID NO:120, nor have they defined "HSPP" by any other means except as SEQ ID NO:120.

Furthermore, Applicants have provided no guidance or working examples of any diseases which are linked to any and all HSPPs, including that of SEQ ID NO:120, nor would it be predictable to the artisan which diseases are linked to HSPP, or can be treated by HSPP compositions. Fin addition, it is not predictable to one of ordinary skill in the art how to use these compositions to treat any and all HSPP-related diseases.

In summary, the breadth is excessive regarding Applicants claiming any and all diseases which are related to any and all HSPPs, including SEQ ID NO:120. No guidance or working examples of pharmaceutical compositions, or methods of treating a disease have been disclosed in the specification, nor would it be predictable to the artisan how to treat any and all diseases related to HSPP expression. Therefore, the Examiner holds that undue experimentation is necessary to practice the invention as claimed.

7. Claim Rejections - 35 USC § 112, first paragraph – written description

A. Claims 21-29, 31, 32, and 36-38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These are genus claims. Polypeptides encoding "**biologically active**" or "**immunogenic**" fragments of SEQ ID NO:120, those which are "**at least 90% identical**" to SEQ ID NO:120 or 254, or for those comprising "**at least 60 contiguous nucleotides**" of SEQ ID NO:254 would have one or more nucleic acid or amino acid substitutions, deletions, insertions and/or additions to said polynucleotide or polypeptide.

The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claims do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the nucleic acid or protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly

variant, SEQ ID NO:120 and 254 alone are insufficient to describe the genus. One of skill in the art would reasonable conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus at the time the invention was made.

8. Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21-29, 31, 32 and 36-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 21-29, 31, 32 and 36-38 are confusing since the metes and bounds of "biologically active" are not known. Applicants have not taught what biological activity is being referred to in these claims.

B. Claims 36-38 are confusing since the metes and bounds of "HSPP" are not known. This term is an acronym and its characteristics have not been specifically defined in the claims or specification.

9. Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

A. Claims 21, 23 and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Blattner et al. (Science 277:1453-1462, 1997). The claims recite an isolated polypeptide comprising a biologically active fragment or an immunogenic fragment comprising at least 5 contiguous residues of SEQ ID

NO:120, as well as its encoding nucleic acid and a composition. Blattmer et al. teach a polypeptide comprising 8 residues of SEQ ID NO:120 (Sequence Comparison A). This fragment would be expected to be immunogenic, which can be considered a biological activity. Though the reference is silent to the encoding nucleic acid sequence, it can be expected that Blattner et al. teach this sequence since they have sequenced the entire genome of E. coli K12. Similarly, the artisan can immediately envision this protein in a pharmaceutically acceptable excipient, such as a buffer or water.

B. Claims 21, 23, 26-28, 32, 36 and 38 are rejected under 35 U.S.C. 102(e) as being anticipated by Rosen et al. (WO200055350). The claims recite an isolated polypeptide comprising a biologically active fragment or an immunogenic fragment comprising at least 5 contiguous residues of SEQ ID NO:120, as well as its encoding nucleic acid. The claims also recite a recombinant polynucleotide, host cell, method of making protein, a polynucleotide comprising at least 60 contiguous bases of SEQ ID NO:254 and a method of treating a disease by administering a composition comprising the polypeptide. Rosen et al. teach a polypeptide which is 99.8% identical to that of SEQ ID NO:120 of the present invention and which comprises approximately 260 contiguous residues of SEQ ID NO:120 (Sequence Comparison B). This fragment would be expected to be immunogenic, which can be considered a biological activity. Furthermore, due to the almost identical sequence of the protein of Rosen to that of the present invention, almost any biological activity which the protein of the present invention has, the protein of Rosen would be expected to have. Rosen et al. also teach a polynucleotide encoding this protein (Sequence Comparison C) and a polynucleotide comprising greater than 600 contiguous bases of SEQ ID NO:254 (Sequence Comparison D – bases ~900-1600). Rosen et al. also teach vectors, host cells and methods of making protein (pages 290-295) as well as therapeutic uses (page 295, line 20 – page 296, line 4, especially page 296, line 4). Due to the length of this patent (~2300 pages), only the pertinent pages have been printed. The artisan can immediately envision this protein in a pharmaceutically acceptable excipient, such as a buffer or water, or those formulations found on pages 290-297.

C. Claims 21, 23, 32 and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Bonaldo et al. (Genome Res. 6:791-806, 1996). The claims recite an isolated polypeptide comprising a biologically active fragment or an immunogenic fragment comprising at least 5 contiguous residues of SEQ ID NO:120, as well as its encoding nucleic acid. The claims also recite a polynucleotide comprising at least 60 contiguous bases of SEQ ID NO:254 and a composition comprising the polypeptide. Bonaldo et al. teach a polynucleotide encoding a polypeptide which is 48% identical to that of SEQ ID NO:120 of the

present invention and which comprises approximately 250 contiguous residues of SEQ ID NO:120 (Sequence Comparison E). This fragment would be expected to be immunogenic, which can be considered a biological activity. Bonaldo et al. also teach a polynucleotide comprising approximately 590 contiguous bases of SEQ ID NO:254 (Sequence Comparison F – bases ~1-590). The artisan can immediately envision the protein encoded for by this polynucleotide in a pharmaceutically acceptable excipient, such as a buffer or water.

10. Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

A. Claims 26-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Blattener et al. or Bonaldo et al. each in view of Sibson et al. (WO 94/01548). The teachings of Blattner and Bonaldo are seen in the above rejection under 35 USC 102. The claims are drawn to host cells and a method of making the protein. Neither Blattner nor Bonaldo teach host cells or a method of making the protein. However, Sibson et al. do teach expression cassettes, host cells and a method of making the protein (page 7, line 39 – page 9, line 10).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the invention of Sibson et al. by substituting a cDNA in the polycloning region of the vector with the polynucleotide (cDNA) of either Blattner or Bonaldo et al. for the purpose of transfecting a host cell as taught by Sibson et al. in view of Sibson et al.'s suggestion that it would be desirable to do so (pages 8-13). One of ordinary skill in the art would have been motivated to make this substitution in order to express the protein encoded by the introduced DNA in a host cell to perform ligand binding and functional assays. There would have been a reasonable expectation of success for a person of ordinary skill in the art to make this invention since these techniques are widely used in the art and are highly successful (Sibson et al., page 10, line 38 – page 12, line 42). The present invention, therefore, is *prima facia* obvious over the above references in the absence of evidence to the contrary.

11. Conclusion

A. No claim is allowable

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
June 27, 2003

ROBERT LANDSMAN
PATENT EXAMINER